REMARKS

A. 35 U.S.C. § 112

The Office Action mailed August 29, 2003 rejected claims 42-55 under 35 U.S.C. 112, second paragraph. These claims have been cancelled without prejudice. Thus, this rejection is moot.

B. 35 U.S.C. § 102

The Office Action has rejected claims 14, 19-23 and 42-51 under 35 U.S.C. § 102(b) as being anticipated by Green et al. (WO9509612). Applicant respectfully traverses this rejection, but submits that this rejection is now moot since claims 14, 19-23 and 42-51 have been cancelled without prejudice. To the extent that the rejection may apply to the newly submitted claims, Applicant respectfully traverses and submits that Green also does not anticipate them

Applicants newly submitted independent claims 70 and 79 recite:

70. A method of killing or inhibiting the proliferation of extracellular microorganisms within the respiratory tract of an animal, the method comprising the steps of:

providing a flow-controlled source of nitric oxide gas;

delivering the nitric oxide gas to the animal's respiratory tract through inhalation; and wherein the inhalation of nitric oxide gas results in direct exposure of nitric oxide gas to the microorganisms within the respiratory tract.

79. A method of suppressing a respiratory infection associated with microorganisms within the respiratory tract of an animal, the method comprising the steps of:

providing a pressurized source of nitric oxide gas;

diluting the nitric oxide gas;

delivering the diluted nitric oxide gas to the animal by inhalation resulting in direct exposure of nitric oxide gas to microorganisms within the animal's respiratory tract.

Green does not disclose the inhalation of nitric oxide gas for killing, inhibiting or suppressing pathogenic microorganisms, as claimed by Applicant. Instead, as the Office Action recognizes, Green "teaches *compositions capable of releasing nitric oxide* and therapeutic methods of use thereof for the treatment of microorganism-related disease states." Office Action, p. 3.

Although the Office Action states that Green "discloses that direct delivery of nitric oxide gas kills *intracellular* pathogens such as *Mycobacterium tuberculosis*," this statement, based on its context, does not teach the delivery of gaseous nitric oxide through inhalation. Rather, Green was describing the *intracellular generation* of nitric oxide gas via enzymatic reaction:

> Nitric oxide gas can be formed metabolically from the amino acid L-arginine through the action of enzyme nitric oxide synthase. Recent evidence show that direct delivery of nitric oxide gas kills intracellular pathogens such as *Mycobacterium tuberculosis.* An ability to specifically deliver compounds capable of releasing nitric oxide to the desired site of infection within the macrophage would greatly enhance killing of intracellular pathogens.

Green, p. 5, ll 6-13 (underlining added).

As seen from the last sentence of quoted paragraph, and from the entirety of Green disclosure and claims, one of ordinary skill in the art cannot but conclude that Green's disclosure is directed toward delivery of specialized compounds other than nitric oxide gas, namely compounds "capable of *releasing* nitric oxide in *aqueous solution*" rather than delivery of nitric oxide gas itself through inhalation.

For example, in its Summary of the Invention section, Green states that "the present invention involves exposing cells to a compound capable of *releasing* nitric oxide *in aqueous solutions, particularly a nitric oxide/nucleophile complex or derivative thereof.*" Green, p. 7, ll. 16-

20 (emphasis added).[1] Additionally and specifically with respect to the respiratory system, Green teaches that one might "aerosolize *closed membranous vesicles* containing nitric oxide *generators* for administration to the respiratory system through inhalation." p. 8, ll. 21-23.[2] Nowhere does Green teach the delivery of *gaseous* nitric oxide through inhalation for inhibiting, killing, or suppressing pathogenic microorganisms, let alone the step of "providing for a flow-controlled source of nitric oxide gas" or "providing for a pressurized source of nitric oxide gas."

In fact, according to Green, "[n]itric oxide in its pure form ... is a highly reactive gas having limited solubility in aqueous media ..., therefore, is difficult to introduce reliably into most biological systems without premature decomposition." Green, p. 4, ll. 13-18. Hence, Green teaches that "[t]he use of [compounds capable of releasing nitric oxide in aqueous solution] in treating animals, particularly humans, circumvents the *disadvantages* of the use of *pure nitric oxide*, ..." Green, p. 21, ll. 35 to 22, ll. 1.

Accordingly, Green cannot anticipate Applicant's newly submitted claims 70 and 79, and their respective dependent claims.

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[1] *See also, e.g.*, p.1, ll. 15-19 ("the present invention is directed to the use of compounds which release nitric oxide in aqueous solutions ..."); p. 8, ll. 12-13 ("object of the invention is to use liposomes containing nitric oxide generators to treat macrophage-based diseases caused by viruses, bacteria, parasites, and fungi."), p. 9, ll. 23-28 ("The present invention is predicated on the discovery that cell proliferation can be attenuated or inhibited by exposing cells to a compound that is capable of releasing nitric oxide in an aqueous solution ...."); p. 3, ll. 17-20; 32-33 ("release nitric oxide in aqueous solution."); p. 4, l. 6 ("nitric oxide solutions..."); p. 6, ll. 5-8 (distinguishing prior art and stating that prior art does not disclose "a preparation of *liposomes* that contain nitric oxide *generators* ....") (emphasis added); p. 41, claim 1 ("a compound capable of releasing nitric oxide in an aqueous solution").

[2] *See also, e.g.*, p. 23, ll.7-10 ("The nitric oxide releasing compounds in the context of the present invention, alone or in combination with other suitable components, can be made into aerosol formulations to be administered via inhalation."); p.27, ll. 35 ("Liposomes are a desirable vehicle for administering nitric oxide generators ...."); p. 29, ll. 14-25 ("Nitric oxide generator-containing vesicles are administered via ... inhalation ...")

C. 35 U.S.C. § 103

The Office Action also rejected claims 24-30, 52-55 under 35 U.S.C. § 103(a) as being unpatentable over Green in view of Blaise (WO 9801142). Applicant respectfully traverses this rejection, but submits that this rejection is now moot since claims 24-30, 52-55 have been cancelled without prejudice. To the extent that the rejection may apply to the newly submitted claims, Applicant respectfully traverses and submits that the Green and Blaise references do not render the claims obvious.

"To establish a *prima facie* case of obviousness, three basic criteria must be met." MPEP § 2143. "First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to ... combine reference teachings." *Id.* "Second, there must be a reasonable expectation of success." *Id.* "Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." *Id.*

The Green and Blaise references failed to establish a prima facie case of obviousness. Among other reasons, there is initially no motivation or suggestion, apart from Applicant's disclosure, to combine Green and Blaise to use nitric oxide gas by inhalation for killing, inhibiting, or suppressing pathogenic microorganisms in the respiratory tract.

"A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." MPEP §2141.02 (original emphasis) citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). As already discussed above, close reading of Green actually teaches away from the use of nitric oxide gas, as opposed to compounds capable of releasing nitric oxide in aqueous solution, to combat microoganism-related diseases. As to Blaise, it teaches the use of nitric oxide to "prevent or control *inflammatory response following extracorporeal blood circulation* in

humans and animals." This has nothing to do with microbial infections. Thus, claims 70 and 79, and their respective dependent claims are allowable over the prior art of record.

D. Claim Objections

Claims 23, 27, 30, 51, and 55 have been cancelled. Thus, objections to these claims are now moot.

E. Support For Newly Added Claims

The newly added claims are adequately supported by the original specification as filed. Examples of the support found in the specification are provided for each claim: claim 70 (p. 16, ll. 24-25; p. 17, ll. 1-2; p. 7, ll. 19-21, 30-32); claims 71 and 72 (p. 9, ll. 4-10); claim 73 (p. 8, l. 32-p. 9, l. 2; p. 16, ll. 28-29); claim 74 (p. 18, ll. 27-28); claim 75 (p. 16. ll. 24-25); claim 76 (p. 5, ll. 18-15; p. 16, ll. 21-25); claims 77 and 78 (p. 9, ll. 4-10); claim 79 (p. 8, ll. 32 to p. 9, ll.2; p. 7, ll. 19-21, 30-32); claim 80 (p. 18, ll. 26-28); claim 81 (p. 10, ll. 29-32); claim 82 (p. 7, ll. 5-12); claim 83 (pp. 17-18); claim 84 (p. 9, ll. 4-10)

V. Conclusion

For the foregoing reasons, Applicant believes that the claims of this application are patentable and respectfully requests the issuance of a Notice of Allowance. If the undersigned can be of any assistance to the Patent Office, a telephone call is respectfully requested.

Respectfully Submitted

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